

Right Coronary Artery Stenosis: An Independent Predictor of Atrial Fibrillation After Coronary Artery Bypass Surgery

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Objectives. This study attempted to determine the importance of severe proximal right coronary artery disease as a predictor of atrial fibrillation in patients after coronary artery bypass surgery.

Background. Studies in patients undergoing noncardiac surgery have suggested that ischemia in the right coronary artery distribution is associated with a high incidence of atrial fibrillation. However, the importance of right coronary artery disease as a predictor of atrial fibrillation after bypass surgery is unknown.

Methods. The occurrence of sustained postoperative atrial fibrillation was studied prospectively in 168 consecutive patients undergoing coronary artery bypass grafting. Patients were followed up postoperatively until discharge. Severe right coronary artery stenosis was defined as $\geq 70\%$ lumen narrowing.

Results. Of 104 patients with proximal or mid right coronary artery stenosis, 45 (43%) had atrial fibrillation postoperatively compared with 12 (19%) of the 64 patients without significant right coronary disease ($p = 0.001$). Univariate predictors of atrial

fibrillation included right coronary artery stenosis ($p = 0.001$), advancing age ($p = 0.0001$) and lack of beta-adrenergic blocking agent therapy after bypass surgery ($p = 0.0004$). Multivariate adjusted risk of developing atrial fibrillation after bypass surgery increased with the presence of severe right coronary artery disease (odds ratio 3.69, 95% confidence interval [CI] 1.61 to 8.48), advancing age (odds ratio 2.24/10 years, CI 1.48 to 3.41) and male gender (odds ratio 2.36, CI 1.01 to 5.49). The use of beta-blockers postoperatively was associated with a protective effect (odds ratio 0.4, CI 0.17 to 0.80).

Conclusions. The presence of severe right coronary artery stenosis is an independent and powerful predictor of atrial fibrillation after coronary artery bypass surgery. In association with age, gender and postoperative beta-blocker therapy, these variables can be used to identify patients at increased risk for developing this arrhythmia.

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Atrial fibrillation is a frequent complication after coronary artery bypass grafting, occurring in up to 40% of patients (1-6). Although this arrhythmia is usually benign, it may result in hemodynamic compromise, thromboemboli and an increase in the hospital length of stay (3,6-9). In addition, treatment of atrial fibrillation may be associated with potentially harmful side effects.

Although atrial fibrillation after coronary bypass surgery has been widely studied, there is little agreement as to the pathogenesis of this arrhythmia. Clinical features that have been identified as predictors of atrial fibrillation include advancing age and lack of postoperative beta-adrenergic blocking agent therapy (3,4). However, in a large number of patients who develop atrial fibrillation, no apparent risk factor can be identified (2,6). In previous studies (3,4,10) the extent and location of coronary artery disease has not been independently predictive of atrial fibrillation after bypass surgery, but limited

information has suggested that concomitant right coronary endarterectomy may predispose to this arrhythmia. Other studies (11-13) of patients undergoing noncardiac surgery have suggested that ischemia in the right coronary artery distribution is also associated with a high incidence of atrial fibrillation. However, the importance of severe right coronary artery disease as a predictor of postoperative atrial fibrillation has not been previously evaluated.

To assess this further, patients undergoing elective coronary artery bypass surgery were prospectively followed up to determine the impact of severe proximal right coronary artery disease on the incidence of postoperative atrial fibrillation. These data, in combination with other perioperative variables, were used to identify patients who were at highest risk for developing atrial fibrillation after bypass surgery.

Methods

Study patients. One hundred sixty-eight consecutive patients undergoing a first coronary artery bypass graft surgery were studied prospectively for the occurrence of postoperative atrial fibrillation. Exclusion criteria included previous history of atrial fibrillation and use of antiarrhythmic agents, with the

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exception of digoxin and beta-blockers. No patient had significant valve disease requiring surgical intervention.

All patients had undergone coronary angiography within 1 month of bypass surgery. Significant right coronary artery disease was defined as $\geq 70\%$ lumen diameter narrowing of the proximal or mid segment. Left ventricular function was assessed by single-plane ventriculography. All angiograms were read by an experienced invasive cardiologist before bypass surgery.

Surgical technique. Coronary artery bypass surgery was performed by one of four cardiothoracic surgeons using standard techniques. After the initiation of cardiopulmonary bypass, cardiac arrest was achieved using cold cardioplegia. The delivery of cardioplegia was by antegrade or a combination of antegrade and retrograde perfusion. Myocardial preservation was maintained by topical cold saline solution. Systemic hypothermia was maintained at 28°C. Conduits for bypass included the saphenous veins or internal mammary artery, or a combination of the two. All patients with significant right coronary artery disease underwent bypass. No patient underwent endarterectomy of the proximal or mid right coronary artery.

Clinical evaluation. All patients had continuous electrocardiographic (ECG) telemetry monitoring (Hewlett-Packard 78510B) for the first 6 postoperative days and, in most patients, until hospital discharge. All stored alarms were reviewed daily by an experienced cardiologist. Sustained atrial fibrillation was defined as an episode lasting >30 min. All atrial fibrillation identified on the monitor was confirmed by a 12-lead ECG. The day of onset and the use of beta-blocker therapy before onset of the arrhythmia were noted. Hospital stay was defined as the total number of days that the patient was hospitalized from the day of surgery.

The relation of atrial fibrillation to several perioperative variables was also evaluated. The preoperative variables examined included age; gender; presence of diabetes, hypertension or chronic obstructive pulmonary disease; coronary anatomy and dominance; left ventricular end-diastolic pressure at time of angiography; left ventricular ejection fraction; and urgency of operation. Intraoperative variables included aortic cross-clamp time, pump time, route of cardioplegia and number of distal anastomoses. Postoperative variables included peak creatinine kinase (CK) level (U/liter); frequency and dose of vasopressors; right- and left-sided cardiac pressures; and prevalence of hypotension, hypoxia and acidosis. In addition, postoperative complications, including new Q wave myocardial infarction, stroke, thoracic reexploration and death, were identified.

Statistical analysis. Patients were grouped according to the presence or absence of right coronary artery disease and development of postoperative atrial fibrillation. Mean values and standard errors were compared for continuous variables and percents for categoric variables. Initial comparisons between groups were made using a Student *t* test for continuous measures and the chi-square test for categoric variables. Independent predictors of atrial fibrillation were determined

Table 1. Clinical Characteristics of Patients With and Without Significant Right Coronary Artery Disease

	With RCA (n = 104)	Without RCA (n = 64)	p Value
Age (yr)	65.8 \pm 1.0	63.6 \pm 1.3	0.2
Male gender	67 (64%)	46 (72%)	0.4
HBP	63 (61%)	34 (52%)	0.4
COPD	11 (11%)	10 (15%)	0.5
LVEF (%)	55.8 \pm 1.5	58.3 \pm 1.6	0.3
No. of grafts	3.3 \pm 0.1	3.3 \pm 0.1	1.0
Clamp time (min)	40.5 \pm 1.1	39.7 \pm 1.6	0.7
Pump time (min)	88.4 \pm 2.0	85.6 \pm 3.1	0.4
CK (U/liter)	1,109 \pm 103	1,408 \pm 175	0.1
Beta-blocker post-op	77 (74%)	49 (77%)	0.9
AF	45 (43%)	12 (19%)	0.001

Data presented are mean value \pm SEM or number (%) of patients. AF = atrial fibrillation; CK = creatinine kinase; COPD = chronic obstructive pulmonary disease; HBP = high blood pressure; LVEF = left ventricular ejection fraction; post-op = postoperatively; RCA = right coronary artery.

by using a stepwise logistic regression analysis that included the following variables: age; gender; hypertension; diabetes; chronic lung disease; coronary anatomy, including right coronary artery stenosis; beta-blocker therapy; number of distal anastomoses; and clamp and pump times. A *p* value < 0.05 was considered statistically significant.

Results

Sustained atrial fibrillation occurred in 57 (33.9%) of the 168 patients a mean of 3.4 ± 0.2 days after coronary artery bypass surgery (range 1 to 7). The clinical characteristics of the patients with and without significant right coronary artery disease are compared in Table 1. There were no significant differences between the two groups with respect to gender; left ventricular ejection fraction; or previous history of diabetes, hypertension or chronic lung disease. The duration of cardiopulmonary bypass and aortic cross-clamping, delivery of cardioplegia and number of distal anastomoses did not differ between the two groups. Peak CK levels and postoperative beta-blocker therapy were also similar. The only variable that differed significantly between the two groups was the frequency of atrial fibrillation. Of 104 patients with significant right coronary artery disease, 45 (43%) had postoperative atrial fibrillation compared with 12 (19%) of the 66 patients without disease in this vessel (*p* = 0.001), a 2.4-fold increase in the incidence of atrial fibrillation.

The contribution of right coronary artery disease is further shown in Table 2 in which patients were stratified according to the occurrence of atrial fibrillation. Right coronary artery disease was present in 45 (79%) of the 57 patients with atrial fibrillation compared with 59 (53%) of the 111 patients without atrial fibrillation (*p* = 0.001). Patients with postoperative atrial fibrillation were also significantly older (*p* = 0.0001) and less likely to have beta-blocker therapy after bypass surgery (*p* =

Table 2. Clinical Characteristics of Patients Stratified According to Occurrence of Atrial Fibrillation

	With AF (n = 57)	Without AF (n = 111)	p Value
Age (yr)	69.7 ± 1.2	62.1 ± 1.0	0.0001
Male gender	41 (72%)	72 (65%)	0.5
HBP	35 (61%)	62 (56%)	0.6
COPD	10 (18%)	11 (10%)	0.2
LVEF (%)	56.7 ± 1.8	56.3 ± 1.4	0.9
RCA stenosis	45 (79%)	59 (53%)	0.001
No. of grafts	3.3 ± 0.1	3.3 ± 0.1	1.0
Clamp time (min)	38.7 ± 1.5	40.6 ± 1.2	0.3
Pump time (min)	84.5 ± 2.9	88.0 ± 2.2	0.2
Peak CK (U/liter)	1,009 ± 135	1,255 ± 12.1	0.2
Beta-blocker post-op	29 (51%)	87 (78%)	0.0004

Data presented are mean value ± SEM or number (%) of patients. Abbreviations as in Table 1.

0.0004). Hospital stay was also significantly longer in patients with (10.1 ± 0.6 days) than without (8.3 ± 0.4 days) atrial fibrillation ($p = 0.02$).

There were no other significant clinical, angiographic or hemodynamic differences between the two groups. The incidence of postoperative stroke, thoracic reexploration and Q wave myocardial infarction in patients with and without atrial fibrillation was 4%, 5% and 5% and 2%, 1% and 5%, respectively. One patient died 3 days after bypass surgery secondary to sudden intractable ventricular arrhythmia. Atrial fibrillation had not occurred before this event.

A stepwise logistic regression analysis was performed to identify which clinical variables were independent predictors of atrial fibrillation after coronary bypass surgery (Table 3). Advancing age was the most powerful predictor of postoperative atrial fibrillation ($p = 0.0002$), with a 2.2-fold increase for every 10-year increase in age. Similarly, the presence of proximal right coronary artery disease was also an important predictor ($p = 0.002$), with the odds of postoperative atrial fibrillation 3.7 times more likely in patients with than without right coronary artery stenosis. There was also a weak association between atrial fibrillation and gender, with men having 2.4 times the odds of developing postoperative atrial fibrillation as women ($p = 0.05$). By contrast, the use of postoperative beta-blockers had a protective effect such that patients treated with beta-blockers had 0.4 times the odds of developing postoperative atrial fibrillation as those untreated ($p = 0.01$).

Table 3. Multivariate Analysis of Predictors of Atrial Fibrillation After Coronary Artery Bypass Graft Surgery

Variable	Unit Increase	Odds Ratio	p Value	95% CI
Age (yr)	10	2.2	0.0002	1.48-3.41
RCA stenosis	1	3.7	0.002	1.61-8.48
Beta-blocker post-op	1	0.4	0.01	0.17-0.80
Male gender	1	2.4	0.05	1.01-5.49

CI = confidence interval; other abbreviations as in Table 1.

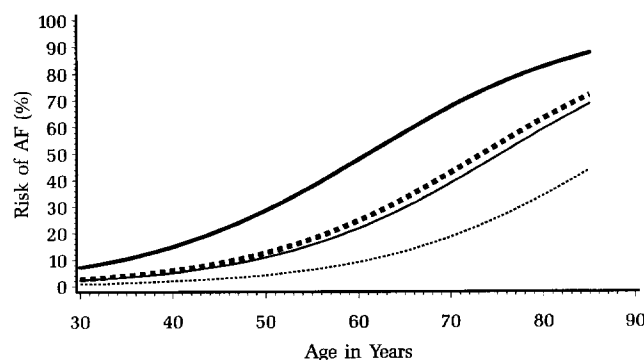
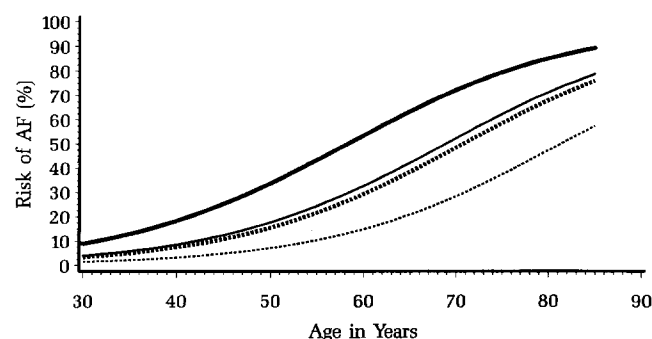


Figure 1. Graphic representation of the logistic regression equation depicting the risk of atrial fibrillation (AF) in all patients stratified according to age, right coronary artery disease and postoperative beta-blocker therapy. **Thick solid line** = right coronary artery disease and no beta-blocker therapy; **thick dotted line** = right coronary artery disease and beta-blocker therapy; **thin solid line** = no right coronary artery disease and no beta-blocker therapy; **thin dotted line** = no right coronary artery disease and beta-blocker therapy.

Although male gender was an independent risk factor for this arrhythmia, the effects of right coronary artery disease and beta-blocker therapy on the development of atrial fibrillation after bypass surgery were similar for both men and women.

The logistic regression equation is represented graphically in Figures 1 and 2 and depicts the relation among the four independent variables of postoperative atrial fibrillation. In Figure 1 patients were stratified according to the presence of right coronary artery disease and postoperative beta-blocker therapy. As depicted by Figure 1, the incidence of atrial fibrillation increased in all four groups with advancing age. However, patients with proximal right coronary artery stenosis without postoperative beta-blocker had the highest occurrence of atrial fibrillation, with the risk ranging from <20% in patients ≤40 years old to >70% in those ≥70 years old. Postoperative beta-blockers did offer some protection in the high risk older patients with right coronary disease such that

Figure 2. Graphic representation of the logistic regression equation depicting the risk of atrial fibrillation (AF) in patients with right coronary artery disease according to age, gender and postoperative beta-blocker therapy. **Thick solid line** = men without beta-blocker therapy; **thin solid line** = women without beta-blocker therapy; **thick dotted line** = men with beta-blocker therapy; **thin dotted line** = women with beta-blocker therapy.



the incidence of atrial fibrillation in this group was similar to that of patients without right coronary artery stenosis not treated with a beta-blocker. The lowest risk patients were those without proximal right coronary artery disease who were treated with a postoperative beta-blocker. The risk of atrial fibrillation in this group at age 70 was only 19%.

Figure 2 depicts the risk of atrial fibrillation in patients with right coronary artery stenosis according to gender and postoperative beta-blocker therapy. The risk of developing atrial fibrillation at any age was highest for men without beta-blocker therapy, with a predicted risk ranging from <20% in men ≤40 years old to >70% in those >70 years old. Men with and women without postoperative beta-blocker therapy had a nearly equal risk of developing atrial fibrillation, with an incidence of ~50% at age 70 years. Women with beta-blocker therapy had the lowest risk of postoperative atrial fibrillation, with a 30% chance of arrhythmia occurrence at 70 years of age. Despite the powerful effect of age on the incidence of atrial fibrillation after bypass surgery, these data show that the presence of proximal right coronary artery disease and the lack of postoperative beta-blocker therapy remain important risk factors for the development of atrial fibrillation.

The effect of the four variables independently predictive of postoperative atrial fibrillation may be represented by the following equation and reflects the probability of developing this arrhythmia:

$$\text{Probability of atrial fibrillation} = e^u / 1 + e^u,$$

where $u = -6.8428 + 0.0808(\text{Age}) + 0.8587(\text{Gender}) - 0.9894(\text{Beta-blocker therapy}) + 1.3069(\text{Right coronary artery stenosis})$.

For Figure 1, gender = 0.673, which is the proportion of men in the study. For Figure 2, gender = 1 for men and 0 for women. Beta-blocker therapy = 1 if used after surgery and before onset of atrial fibrillation, if it occurred, and 0 if not used or started after the initiation of atrial fibrillation. Right coronary artery stenosis = 1 if present and 0 if not present.

Discussion

Atrial fibrillation is one of the most common arrhythmias complicating coronary artery bypass surgery, with a reported incidence of up to 40% (1–6). Despite the frequent occurrence of atrial fibrillation after cardiac surgery, little is known about the pathogenesis of this arrhythmia. In the present prospective study, risk factor analysis identified the presence of severe proximal right coronary artery disease as an independent and powerful predictor of atrial fibrillation after bypass surgery, an observation that has not been previously demonstrated. In addition, and consistent with previous studies, age, male gender and lack of postoperative beta-blocker therapy also proved to be important determinants of postoperative atrial fibrillation. Using these predictors in combination, subgroups of patients with a high risk of developing atrial fibrillation after coronary artery bypass surgery can be identified. Elderly patients with significant right coronary artery disease were at

highest risk for atrial fibrillation after bypass surgery, with men being more predisposed to this arrhythmia than women. Despite the high risk of postoperative atrial fibrillation in these groups with right coronary artery disease, postoperative beta-blocker therapy remained an effective means of reducing the frequency of this arrhythmia in both men and women and in the older age groups.

Previous studies. Few studies in the past have used risk factor analysis to predict which patients are at high risk for developing atrial fibrillation after bypass surgery (3,4,6,14). In a large study by Fuller et al. (3), the relation between postoperative atrial fibrillation and 25 perioperative variables was evaluated in patients undergoing bypass surgery. Multivariate regression analysis revealed that the strongest independent predictors of postoperative atrial fibrillation were advancing age ($p = 0.0001$), lack of postoperative beta-blocker therapy ($p = 0.001$) and male gender ($p = 0.02$). In a similar analysis, Leitch et al. (4) found that in patients undergoing coronary artery bypass graft surgery at their institution, age was the most important predictor of atrial fibrillation, with a 1.7-fold increase in the risk of atrial fibrillation for every 10-year incremental increase in age. Other variables that had an independent influence on the development of atrial fibrillation included obstructive pulmonary disease ($p = 0.006$) and chronic renal disease ($p = 0.04$). Patients were not stratified according to the presence of right coronary artery disease in either of these studies. However, Caretta et al. (14) found that of 236 consecutive patients undergoing coronary artery bypass, the presence of right coronary artery occlusion in combination with proximal left anterior descending coronary artery stenosis was not a risk factor for atrial fibrillation. In that study only a prolonged cross-clamp time was associated with postoperative atrial fibrillation.

The protective effect of beta-blocker therapy after bypass surgery has been demonstrated by several studies (6,15,16). Rubin et al. (6) demonstrated that of 123 patients undergoing coronary artery bypass surgery, 16.2% of patients treated with propranolol developed postoperative atrial fibrillation compared with 37.5% of control patients ($p < 0.03$). Although patients with atrial fibrillation were older than patients without this arrhythmia, this difference did not reach statistical significance. Another agent that may also be effective in preventing atrial fibrillation is sotalol (17,18). In a study by Nystrom et al. (18), 101 patients undergoing coronary artery bypass grafting were randomized to receive sotalol or another beta-blocker. The incidence of atrial fibrillation was 10% in the sotalol group compared with 29% in the other beta-blocker group ($p = 0.03$). Similar to previous studies, older age was also a predictor of postoperative atrial fibrillation. In neither of these two studies (6,18) was the importance of right coronary artery disease to the incidence of postoperative atrial fibrillation evaluated.

Potential mechanism. In the present study the mechanism by which proximal right coronary artery stenosis may predispose to atrial fibrillation remains unknown. Previous studies have suggested that intraoperative ischemia in the right coro-

nary distribution may be important in the pathogenesis of this arrhythmia. In patients undergoing bypass surgery, concomitant right coronary endarterectomy has been associated with a high incidence of postoperative atrial arrhythmias (10). Pattison et al. (10) found that in 200 patients undergoing coronary artery bypass surgery, the incidence of supraventricular arrhythmias, the majority of which were atrial fibrillation, was 32% in patients undergoing both bypass surgery and right coronary endarterectomy but only 19.8% in patients undergoing bypass surgery alone. These investigators suggested that ischemia secondary to endarterectomy may be the reason for this observation.

In studies unrelated to cardiac surgery, atrial fibrillation has been associated with right atrial and right ventricular infarctions accompanying an acute myocardial infarction. Several investigators (11,12) have reported that supraventricular arrhythmias, especially atrial fibrillation, are the most frequent ECG abnormality associated with atrial infarctions. In addition, the majority of these infarctions appear to be localized to the right atrium and are frequently associated with proximal right coronary artery disease (11,12). Similarly, ischemia resulting in right ventricular dysfunction may also play a role in the pathogenesis of atrial fibrillation. Rechavia et al. (13) found that the presence of reduced right ventricular systolic function in patients with a first inferior myocardial infarction was an independent predictor of atrial fibrillation during the first 24 h of infarction. Potential mechanisms to explain this finding included concomitant right atrial infarction or an increase in right atrial pressure or size secondary to elevated right ventricular filling pressures. Unlike atrial fibrillation associated with an acute myocardial infarction, the peak incidence of atrial fibrillation after coronary artery bypass grafting is usually 48 to 72 h after operation, suggesting that in addition to right coronary artery disease, other factors are important in the pathogenesis of this arrhythmia. The mechanism by which right coronary artery disease may predispose to postoperative atrial fibrillation will require further perioperative investigation.

Clinical implications. The importance of proximal right coronary artery disease as an additional risk factor for postoperative atrial fibrillation is further highlighted by its association with a prolonged hospital stay (10.1 ± 0.6 vs. 8.4 ± 0.4 days, $p = 0.02$). Although further studies are necessary to determine whether atrial fibrillation is a causal or confounding factor, this observation does suggest that prevention of this arrhythmia may impact hospital stay and costs. Risk stratification of patients undergoing bypass surgery may help to identify those patients most likely to benefit from prophylactic therapy. Whether the prevention of atrial fibrillation will impact hospital stay and costs will need to be studied further by controlled trials.

Conclusions. We believe that this is the first study to identify right coronary artery stenosis as a risk factor for atrial fibrillation after coronary artery bypass grafting. Additional

independent and additive predictors are advancing age, male gender and lack of postoperative beta-blocker therapy. This study also confirms that beta-blockers reduce the incidence of atrial fibrillation after bypass surgery. Whether such therapy will be beneficial in all risk groups has yet to be determined by future controlled trials. However, even a modest reduction in the incidence of atrial fibrillation after coronary artery bypass surgery may have a significant impact on postoperative course and may reduce hospital stay.

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